CLAIMS

1. A yeast cell having a pheromone system, which cell expresses (a) a heterologous surrogate of a yeast pheromone system protein, said surrogate, under at least some conditions, performing in the pheromone system of the yeast cell a function naturally performed by the corresponding yeast pheromone system protein, and (b) a heterologous peptide, whereby if said peptide modulates the interaction of said surrogate with said pheromone system, said modulation is a selectable or screenable event.

2. The yeast cell of claim 1 wherein the endogenous pheromone system protein is not produced in functional form.

3. The yeast cell of claim 1 wherein the peptide is secreted by the cell into the periplasmic space, from which it interacts with said surrogate.

4. The yeast cell of claim 3, wherein the peptide is expressed in the form of a precursor peptide comprising a cleavable leader peptide and a mature peptide, and the leader peptide is substantially homologous to the leader peptide of the wild-type pheromone of said cell.

5. The yeast cell of claim 4 wherein the wild-type leader peptide is that of the Saccharomyces cerevisiae α factor or a-factor.

6. The yeast cell of claim 4 in which the wild-type

pheromone is not secreted.

7. The yeast cell of claim 3 wherein the peptide is also expressed in a nonsecretory form.

8. The yeast cell of claim 1 wherein the cell is a mutant strain having a reduced propensity, relative to the wild-type strain, to have its pheromone signal pathway desensitized through repeated or prolonged stimulation thereof.

9. The yeast cell of claim 8 in which the SST2 gene is not functionally expressed.

10. The yeast cell of claim 1, in which the FAR1 gene is not functionally expressed.

11. The yeast cell of claim 1, further comprising a selectable marker that is activated by the pheromone signal pathway.

12. The yeast cell of claim 11, said selectable marker comprising a pheromone-responsive promoter which is substantially homologous with an endogenous pheromone-responsive promoter, operably linked to a foreign selectable gene.

13. The yeast cell of claim 12 wherein the selectable gene is an IGP dehydratase gene.

14. The yeast cell of claim 12 wherein the homologous wild-type promoter is the FUS1 promoter.

15. The yeast cell of claim 1 wherein the cells belong to the species Saccharomyces cerevisiae.

16. The yeast cell of claim 1 in which the pheromone system protein is a farnesyltransferase.

17. The yeast cell of claim 1 in which the pheromone system protein is a carboxymethyltransferase.

18. The yeast cell of claim 1 in which the pheromone system protein is a kinase.

19. The yeast cell of claim 1 wherein the yeast pheromone system protein is a protease involved in the production of the mature form of the yeast pheromone, through the cleavage of a precursor protein, and the surrogate is also a protease.

20. The yeast cell of claim 19 wherein the precursor protein produced in the cell is itself a surrogate of the yeast pheromone precursor protein, and said surrogate precursor protein has an amino acid sequence comprising a recognition site recognized by the surrogate protease, said recognition site differing from that recognized by the yeast pheromone system protease, but said surrogate precursor protein is cleaved by the surrogate protease to produce the mature form of the yeast pheromone.

21. The yeast cell of claim 20 wherein the wild type yeast pheromone precursor protein is not produced.

22. The yeast cell of claim 1 wherein the yeast

pheromone system protein is an ABC transporter involved in the membrane transport of the yeast pheromone, and the surrogate is also an ABC transporter.

23. The yeast cell of claim 22 wherein the surrogate transports the yeast pheromone unless the peptide interferes with such transport.

24. The yeast cell of claim 22 wherein the surrogate transports the yeast pheromone only with the aid of said peptide.

25. The yeast cell of claim 1 wherein the yeast pheromone system protein is the yeast pheromone receptor.

26. The yeast cell of claim 25 in which the peptide is an agonist for the surrogate receptor.

27. The yeast cell of claim 25 in which the peptide is an antagonist for the surrogate receptor.

28. The yeast cell of claim 25 wherein the Gα subunit of the G protein is chimeric.

29. The yeast cell of claim 28 wherein the amino terminal portion of the Gα subunit is substantially homologous with the Gα subunit of a yeast G protein and the remainder is substantially homologous with the corresponding portion of a Gα subunit of a heterologous G protein.

30. The yeast cell of claim 1 in which the pheromone system protein is a cyclin.

31. The yeast cell of claim 30, said yeast cell further containing a non-pheromone-responsive screenable marker.

32. A yeast culture comprising a plurality of yeast cells according to claim 1, said yeast cells collectively expressing a peptide library.

33. A method of assaying a peptide for modulation of the activity of a non-yeast surrogate for a pheromone system protein which comprises providing yeast cells according to claim 1, which cells functionally express said surrogate and said peptide, and determining whether the pheromone signal pathway is activated or inhibited by said peptide.

34. The method of claim 33 in which the cells comprise a pheromone-responsive selectable marker, and cells are selected for expression of a peptide having the desired activating or inhibiting effect.

35. The method of claim 33 in which the cells comprise a pheromone-responsive screenable marker, and cells are screened for expression of a peptide having the desired activating or inhibiting effect.

36. A method of assaying a peptide library for activity of a non-yeast pheromone system protein surrogate which comprises providing a yeast culture according to claim 32, whose cells each functionally express said surrogate and a peptide of said library,

said culture collectively expressing the entire peptide library, and determining whether the pheromone signal pathway is activated or inhibited by said peptides in each of the cells of said culture.

37. The method of claim 34 in which the surrogate is human Mdr1, the cells grow on histidine-free media only if the surrogate transports α-factor, the cells are galactose-sensitive only if the surrogate transports α-factor, and endogenous pleiotropic drug resistance genes have been inactivated.

38. The yeast cell of claim 25 wherein the surrogate receptor is the C5a receptor.

39. The cell of claim 1 wherein the cognate yeast PSP is one involved in the upstream processing of the pheromone prior to its interaction with the receptor.

40. The cell of claim 1 wherein the cognate yeast PSP is involved in the post-transitional modification of the pheromone precursor to yield the mature pheromone.

41. The cell of claim 1 wherein the cognate yeast PSP is involved in the secretion or transport of the pheromone.

42. The cell of claim 1 wherein the cognate yeast PSP is involved in the downstream transduction of a signal received by the pheromone receptor.